Safety Data Sheet

N-Nitroso-N-ethylurethane

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, MUTAGENIC, AND TERATOGENIC. ALKALINE HYDROLYSIS PRODUCES DIAZOETHANE, WHICH IS A HIGHLY TOXIC, IRRITATING, CARCINOGENIC, HIGHLY FLAMMABLE, AND EXPLOSIVE GAS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

N-Nitroso-N-ethylurethane (ENUT) is toxic, carcinogenic, and mutagenic in experimental test systems and teratogenic in rats. Its primary use is for tumor induction and related research in experimental animals and as a research mutagen.

B. Chemical and Physical Data

1. Chemical Abstract No.: 614-95-9

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2. Synonyms:

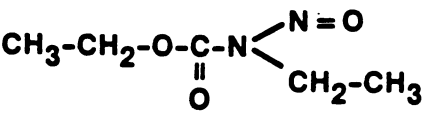
ENUT N-Ethyl-N-nitrosourethane

NEU N-Nitroso-N-ethylurethane

NEUT Ethyl N-ethyl-N-nitrosocarbamate

Ethylnitroso-carbamic acid, ethyl ester (9CI)

3. Molecular formula: $C_5H_{10}N_2O_3$

structure: 

weight: 146.17

4. Density: No data.

5. Absorption spectroscopy: IR, UV, NMR spectra have been reported by Heyns and Roper (1974). UV (CH_2Cl_2): λ (log ε) = 236 (3.85), 403 (2.10), and 422 (2.10) (Mirvish, 1971).

6. Volatility: Concentration of saturated vapor, < 1,000 ppm (estimated). From the boiling point and by analogy with N-nitroso-N-methylurethane, this compound is probably highly volatile at room temperature.

7. Solubility: Slightly soluble in water; soluble in most polar organic solvents.

8. Description, appearance: Pink liquid.

9. Boiling point: 52.5-53.5°C at 5 mm Hg.

Melting point: No data.

10. Stability: Light sensitive in aqueous solution (McCalla et al., 1968). Stability of aqueous solutions is pH dependent (Druckrey et al., 1967). Fairly stable at pH 6-7. Store in the dark at less than -10°C.

11. Chemical reactivity: ENUT is an alkylating agent. It is hydrolyzed by strong alkali (liberating diazoethane, a highly toxic gas) and by strong acid. Reacts with thiol compounds.

12. Flash point: No data.

13. Autoignition temperature: No data.

14. Flammable limits: No data.

Fire, Explosion, and Reactivity Hazard Data

1. Dry chemical or carbon dioxide extinguishers may be used. Fire fighters should wear air-supplied respirators with full-face masks.

2. Decomposition products may be explosive. Sealed bottles at room temperature may explode due to gas pressure.

3. Sensitive to light and moisture.

4. Incompatible with water.

5. Alkaline hydrolysis produces diazoethane, which is a highly toxic, irritating, flammable, and explosive gas.

6. Avoid contact with alkaline solutions.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving ENUT.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by ENUT or the materials used for cleanup. If more than 10 ml has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with a polar organic solvent, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing ENUT shall be disposed of in sinks or general refuse. Surplus ENUT or chemical waste streams contaminated with ENUT shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing ENUT shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing ENUT shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with ENUT shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be

handled in accordance with the chemical waste disposal system. Radioactive waste containing ENUT shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store working quantities of ENUT and its solutions in a safety refrigerator in the work area. Store stocks of ENUT below -10°C in amber bottles with caps and Teflon cap liners. Do not store in ampoules since these could explode. Avoid exposure to light and moisture.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: No data.

2. Separation and analysis: ENUT can be separated from mixtures by high-speed/high-pressure liquid chromatography (Heyns and Roper, 1974). It can be determined with a thermal energy analyzer (Fine et al., 1975). ENUT is also readily determined colorimetrically as nitrite after acid hydrolysis (Preussmann and Schaper-Druckrey, 1972), and, while the yield of nitrite is only 50% of theoretical, it appears to be quite consistent.

Biological Effects (Animal and Human)

1. Absorption: No data. In analogy with N-nitroso-N-methylurethan it is probably absorbed after ingestion and parenteral injection

2. Distribution: No data. Using the same analogy, ENUT is likely to be distributed to organs such as brain, liver, kidney, and pancreas after ingestion.

3. Metabolism and excretion: Few data. It may be assumed that ENUT reacts with tissue constituents to form ethylcarbonium ion that ethylates proteins and nucleic acids. Excretion products have not been identified.

4. Toxic effects: The acute LD50 is 160 mg/kg (rat, intravenous). High doses in rats, after intraperitoneal injection, produce lung edema and congestion.

5. Carcinogenic effects: Chronic oral administration of ENUT to rats and mice results in carcinomas of the forestomach and less frequently in tumors of the lung, thyroid, and esophagus.

6. Mutagenic and teratogenic effects: ENUT is a strong mutagen in plants; no mutagenicity in experimental animals has been demonstrated. However, it is teratogenic when given intravenously to pregnant rats.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Vomiting might reexpose the mouth and esophagus. Drink milk; it may react with nitrosamides. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

References

Druckrey, H., R. Preussmann, S. Ivankovic, and D. Schmähl. 1967. Organotropic carcinogenic action of 65 different N-nitroso compounds with BD rats. Z Krebsforschung 69:193-201.

Fine, D.H., F. Rufeh, D. Lieb, and D.P. Rounbehler. 1975. Description of the thermal energy analyzer TEA for trace determination of volatile and nonvolatile N-nitroso compounds. Anal Chem 47:1188-1190.

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Mirvish, S.S. 1971. Kinetics of nitrosamide formation from alkylureas, N-alkylurethans, and alkylguanidines: Possible implications for the etiology of human gastric cancer. J Natl Cancer Inst 46:1183-1193.

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